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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/297,877	06/28/99	LEE	V PENN-0583

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EXAMINER	
BUNNER, B	
ART UNIT	PAPER NUMBER
1647	11

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/297,877	Applicant(s) LEE ET AL.	
	Examiner Bridget E. Bunner	Art Unit 1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 April 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3* is/are pending in the application.

4a) Of the above claim(s) *1 and 3* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims *1-3* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5* .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group II, claim 2, drawn to a method of diagnosing Alzheimer's disease in a patient comprising detecting in the patient an agent identified to increase processing of amyloid precursor protein in Paper No. 9 (16 April 2001) is acknowledged. The traversal is on the ground(s) that each of the claims is related to the identification of agents which modulate formation of amyloid β peptides found in the endoplasmic reticulum of Alzheimer's patients. Applicant also indicates that the differences in the technical relationship shared between Groups I, II, and III meets the unity of invention requirements of PCT Article 13.2. This is not found persuasive because the inventions in Groups I, II, and III do not relate to a single inventive concept under PCT Rule 13.1, because, under PCT Rule 13.2, they lack the same special technical features. For example, Group I recites the special technical feature of identifying agents which increase or decrease processing of amyloid precursor protein into amyloid β peptides by contacting NT2N cells with a compound and measuring levels of amyloid β peptides formed in the endoplasmic reticulum, which is not required for the methods of groups II and III. Group II recites the special technical feature of diagnosing Alzheimer's disease in a patient comprising detecting in the patient an agent identified to increase processing of amyloid precursor protein into amyloid β peptides, which is not required for the methods of groups I and III. Group III recites the special technical feature of inhibiting processing of amyloid precursor protein into amyloid β peptides comprising administering to a patient an agent that decreases processing of amyloid precursor protein into amyloid β peptides, which is not required for the methods of groups I and II. Further, as

discussed in the previous Office Action (Paper No. 9, 14 March 2001), Werkin et al. (Proc Natl Acad Sci USA 90: 9513-9517, 1993) teaches the invention of Group I and renders claim 1 not novel. Therefore, the technical feature of claim 1 is not a contribution over the prior art and is not considered a special technical feature under PCT Rule 13.1 and 37 CFR § 1.475.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1 and 3 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected group, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 10 (16 April 2001).

Claim 2 is under consideration in the instant application.

Status of Application, Amendments, and/or Claims

The Applicant's response to the Notice to Comply with Sequence Listing Requirements under 37 CFR §1.821 (Paper No. 7, 19 October 2000) has been considered and is found persuasive. Therefore, the requirements set forth in the Notice to Comply (Paper No. 6, 02 October 2000) are withdrawn.

Specification

1. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

2. The disclosure is objected to because of the following informalities:

2a. If applicant desires priority under 35 U.S.C. 120 based upon a previously filed copending application, specific reference to the earlier filed application must be made in the instant application. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph. The status of nonprovisional parent application(s) (whether

patented or abandoned) should also be included. If a parent application has become a patent, the expression "now Patent No._____" should follow the filing date of the parent application. If a parent application has become abandoned, the expression "now abandoned" should follow the filing date of the parent application.

2b. The use of the trademarks IMAGEQUANT and SEPHAROSE have been noted in this application (see pg 15, line 23; pg 16, lines 1,4,7). They should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Appropriate correction is required.

Claim Objections

3. Claim 2 is objected to because of the following informalities:

Claim 2 depends from claim 1, which is currently withdrawn. Appropriate correction is required.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claim 2 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 2 is directed to a method of diagnosing Alzheimer's disease in a patient comprising detecting an agent identified to increase processing of amyloid precursor protein into amyloid β peptides found in neuritic plaques and vascular deposits that accumulate in brains of patients with Alzheimer's disease.

The specification teaches the utilization of the NT2N cell system to study amyloid precursor protein (APP) processing in neurons. The experiments in the instant invention indicate that γ-secretase, which produces $A\beta_{42}$ (a species of Aβ that is 42 amino acids long), is active in the endoplasmic reticulum (ER). Further, experiments also demonstrate that the N-terminal fragment, APPβ, is produced by β-secretase intracellularly in NT2N cells prior to secretion (pg 4, lines 12-21). The specification also teaches that "agents which modulate APP processing by increasing or decreasing production of APPβ and $A\beta_{42}$ can be identified by determining their effects on levels of APPβ and $A\beta_{42}$ produced by β- and γ-secretases in the ER of neuronal cells such as NT2N cells....Agents identified by this method to inhibit levels of APPβ and/or $A\beta_{42}$ produced by these enzymatic pathways may be useful in treating Alzheimer's disease while agents which increase levels of APPβ produced by this pathway may be causative factors in the development of Alzheimer's disease" (pg 13, lines 26-36). However, the specification does not disclose a method of diagnosing Alzheimer's disease in a patient comprising detecting in the patient an agent identified to increase processing of APP into Aβ peptides. The specification does not disclose any agent or compound that increases the processing of APPβ into Aβ peptides. To identify one in the absence of any guidance is undue experimentation. Further, the specification does not teach any specific methodology or working examples to demonstrate how the unspecified agent is identified in the patient. For example, is the diagnostic test performed *in*

vivo or are cells, tissues or bodily fluid taken from the patient? What tissues, cells, or bodily fluid are used for the diagnostic test? What type of test is performed—an X-ray, an enzyme assay, an immune assay, among many others? Also, the state of the art is such that the search for highly specific and sensitive biochemical markers of Alzheimer's disease has been disappointing (Diaz-Arrastia, R. Arch Neurol 58: 354-355, 2001; pg 354, pp 3). "Studies of cerebrospinal fluid (CSF) or blood levels of Aβ1-40 [$A\beta_{40}$] and Aβ1-42 [$A\beta_{42}$], tau protein, neuronal thread protein, apolipoprotein A1 (ApoAI), hemeoxygenase, and APP isoform ratios show significant differences between AD and control subjects, but there is significant overlap between the 2 groups and the magnitude of the differences is rather modest. Some of these markers have not been tested on mildly impaired patients or on patients with non-AD neuropathological conditions" (pg 354, col 1-2; Table).

Due to the large quantity of experimentation necessary to identify an agent that increases processing of APPβ into Aβ peptides and to diagnose Alzheimer's disease by detection of an agent in a patient, the lack of direction/guidance presented in the specification regarding the same, the absence of working examples directed to the same, the complex nature of the invention, and the unpredictability of the agent to diagnose Alzheimer's disease (see discussion and recited reference), undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claim 2 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6. Claim 2 is indefinite because the claim does not have a step that clearly relates back to the preamble. For example, there is no step indicating if the agent must be present at increased or decreased levels to diagnose Alzheimer's disease.

Conclusion

No claims are allowed.

The art made of record and not relied upon is considered pertinent to applicant's disclosure:

U.S. patent 5,262,332

U.S. patent 5,547,841

U.S. patent 5,593,846

U.S. patent 5,837,473

U.S. patent 5,837,672

U.S. patent 6,114,133

Chyung et al. J Cell Biol 138(3): 671-680, 1997.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (703) 305-7148. The examiner can normally be reached on 8:00-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (703) 308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Elizabeth C. Kunnees

Bridget E. Bunner
Art Unit 1647
May 8, 2001